

A Rare Case of Malignant Pleural Mesothelioma with Metastases to the Pancreas Concurrently Diagnosed with Invasive Ductal Adenocarcinoma

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INTRODUCTION

Malignant pleural mesothelioma (MPM) is a rare and aggressive tumor arising from the pleural membranes. The pathogenesis of MPM carries a prolonged latency period (20 to 30 years) following exposure to asbestos, its most prominent risk factor.¹ Although uncommon, its incidence rate has been rising steadily over the last two decades reaching, on average, 2,000 cases per year in the United States.² MPM generally is localized to the ipsilateral lung and lymph nodes. However, metastases infrequently may occur to the contralateral lymphatic system, liver, spleen, thyroid, and brain.³ Multiple treatment modalities are available, however, none are curative and prognosis is very poor.⁴ We present an unusual case of malignant pleural mesothelioma with metastasis to the pancreas diagnosed concurrently with infiltrative ductal adenocarcinoma of the breast, who is doing well 55 months after diagnosis.

CASE REPORT

A 61-year-old female with no past medical history was hospitalized for acute abdominal pain. She was febrile, tachycardic, and normotensive. Physical exam was remarkable for left lower quadrant tenderness. Laboratory work-up revealed a white blood cell count of 15,000 cells/mm³. Computed tomography (CT) of her abdomen was consistent with acute diverticulitis. A mass in the left lingula measuring 3.2 x 2 cm and a subareolar right breast mass were detected incidentally as well.

CT scan of the chest showed a peripheral left lung mass with enlarged left mediastinal and hilar lymph nodes and two densities in the right lung. CT-guided lung biopsy revealed pleural mesothelioma, epithelioid-type. The patient had no history of exposure to asbestos. To evaluate the breast mass further, a mammogram, followed by ultrasound-guided biopsy, was performed. The histology revealed infiltrative ductal adenocarcinoma (ER/PR negative, HER2/Neu positive). Positron emission tomography (PET) scan showed increased hypermetabolic activity in the right axillary lymph nodes in addition to the findings noted during the initial work-up. Whole body bone scan and magnetic resonance imaging (MRI) of the brain did not reveal any further suspicious lesions.

She underwent a radical right mastectomy with right axillary lymph node resection. Chemotherapy was initiated with Pemetrexed for mesothelioma and a combination of Carboplatin, Pertuzumab, and Trastuzumab for the breast malignancy. Follow-up full body PET/CT scans showed a significant reduction in size and metabolic

activity of the left lung mass, resolution of the left hilar, left mediastinal, and right axillary hypermetabolic activities and a decrease in size of the right lung nodule. The patient continued chemotherapy and was monitored with serial imaging for recurrence.

Two years following diagnosis and treatment, a mass in the distal body and tail of the pancreas measuring 1.8 x 1.6 cm was noted on imaging. Sampling of the tumor was obtained by fine needle aspiration via endoscopic ultrasound (Figure 1). Pathology was consistent with metastatic MPM (Figures 2 - 5).

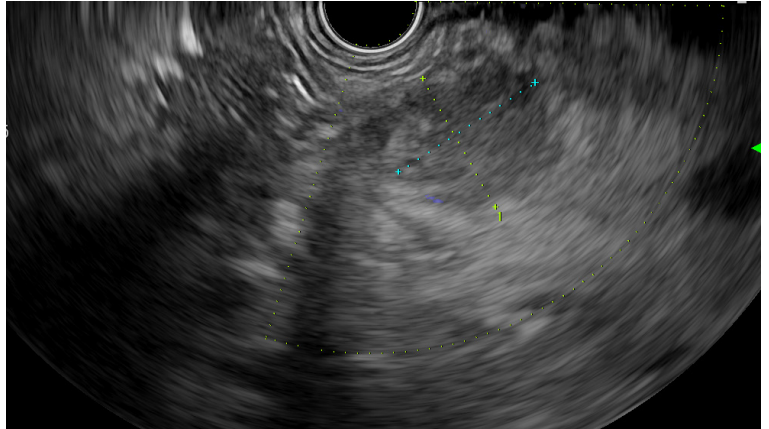


Figure 1. Endoscopic ultrasound shows the pancreatic mass measuring 1.68 x 1.86 cm.

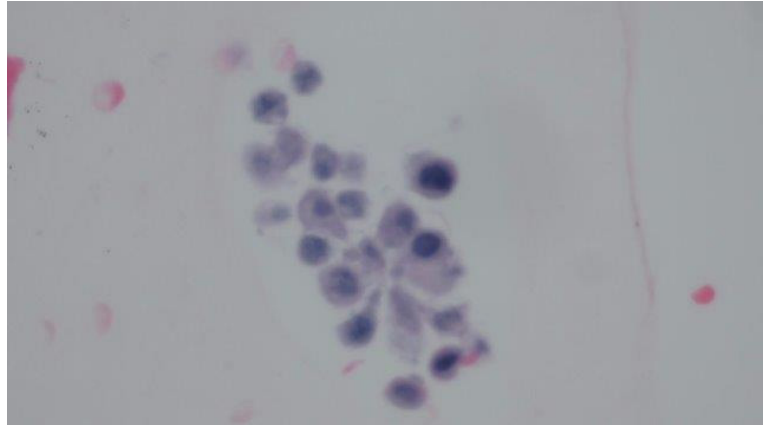


Figure 2. Histology slide shows atypical cells epithelioid mesothelioma by Hematoxylin and Eosin stain (magnified 60x).

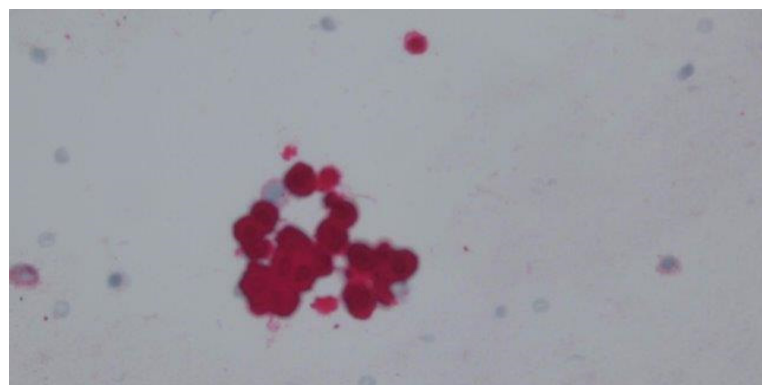


Figure 3. Histology slide shows positive reactivity to calretinin protein (magnified 40x).

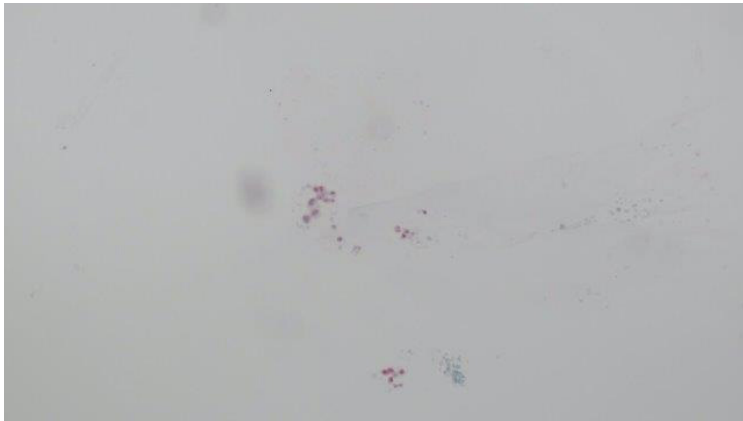


Figure 4. Histology slide shows positivity reactivity to WT1 protein (magnified 10x).

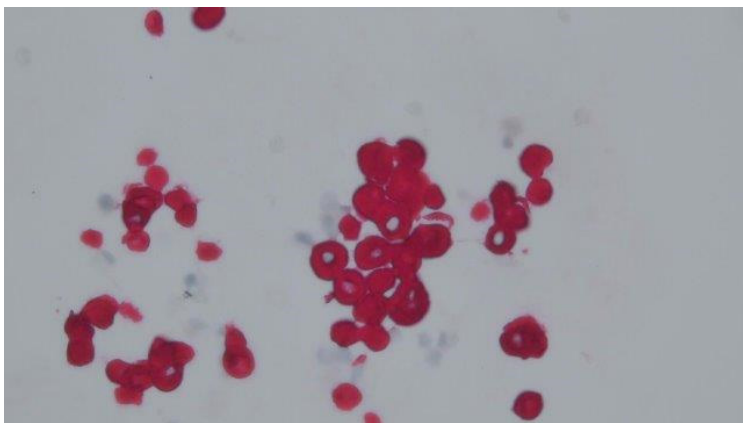


Figure 5. Histology slide shows positive reactivity to cytokeratin 7 (magnified 40x).

DISCUSSION

MPM is considered an uncommon cancer. Its incidence is estimated at 3 per 100,000 individuals.⁵ It includes four histological variants: sarcomatoid, epithelioid, biphasic, and desmoplastic.^{6,7} The vast majority of patients with MPM have a history of exposure to asbestos, at least 20 to 40 years prior to diagnosis. Other risk factors include exposure to erionite and chest wall radiation.⁵

Treatment options are widely variable, with physicians generally opting for a multimodal approach that includes chemotherapy, radiotherapy, and/or surgery. However, no curative regimen exists as MPM carries a devastating prognosis regardless of the treatment given.² In a retrospective cohort study that included 8,740 cases of MPM, the overall median survival was 10 months with a one-year survival of 40% and a three-year survival of 12%, regardless of the treatment given (or lack thereof).^{8,9} Another large retrospective study analyzed a database that included 19,134 cases of MPM and showed that patients treated with all three modalities had better survival outcomes than those untreated. However, the median survival of treated patients was 20 months.²

MPM is usually a localized tumor and most metastatic cases were discovered postmortem by autopsy.³ The contralateral lung, liver, spleen, thyroid, and brain were among the most frequent sites of

distant dissemination. A few reported cases described unusual sites of metastases, such as the salivary glands, stomach, duodenum, ileum, and rectum.¹⁰⁻¹³ However, only one case of MPM with metastasis to the pancreas was described in the literature.¹⁴

Metastasis to the pancreas from any primary source is by itself a rare occurrence, and accounts for 2% to 5% of all pancreatic malignancies.¹⁵ The majority of secondary pancreatic lesions are of epithelial origin. When a hematopoietic origin is identified, sources may include melanoma, sarcoma, or mesothelioma. Among the three possible hematopoietic origins mesothelioma is the least common.¹⁶ Not only are gastrointestinal metastases from MPM rare, but secondary tumors of the pancreas are also uncommon.

The incidence of MPM a few years following treatment of breast cancer with radiation and chemotherapy has been described,¹⁷⁻¹⁹ however, none have reported concurrent incidence of both primary malignancies. Genetic alterations commonly observed in both entities separately could have contributed to the development of both cancers concurrently. The downregulation or suppression of the transforming growth factor β (TGF- β) gene could have been mutated in this case. The TGF- β induced product has been shown to inhibit cell proliferation by delaying the G1-S stage and suppressing the development of mesothelial cells and breast cancer cells.²⁰ Another study showed that the methylation of p57 KIP 2 gene, a cyclin dependent kinase inhibitor, leading to its downregulation and inhibition of its tumor suppressing properties, also was described in breast and lung cancers.²¹ Although no correlation between tumor pathogenesis and human leucocyte antigen-G expression has been identified yet, this gene was expressed more frequently and focally on mesothelial and breast cancer cells compared to normal cells.²²

To the best of our knowledge, the patient described in this case report represented the second case of MPM with metastases to the pancreas. She also was the first patient diagnosed with multiple primary malignancies that includes MPM and infiltrative ductal adenocarcinoma. Despite having multiple malignancies at an advanced stage, this patient was still alive 5.5 years following diagnosis.

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